

Claims

1. A replication defective recombinant adenovirus comprising at least one DNA sequence encoding the whole,
5 or an active part, of GDNF or a derivative thereof.
2. An adenovirus according to Claim 1, wherein the DNA sequence contains a secretory sequence in the 5' position and in reading frame with the sequence encoding GDNF.
3. An adenovirus according to Claim 1, wherein the DNA
10 sequence is a cDNA sequence.
4. An adenovirus according to Claim 1, wherein the DNA sequence is a gDNA sequence.
5. An adenovirus according to Claim 1, wherein the DNA sequence encodes human GDNF.
- 15 6. An adenovirus according to Claim 1, wherein the DNA sequence is under the control of signals enabling expression in nerve cells.
7. An adenovirus according to Claim 6, wherein the expression signals comprise a viral promoter
- 20 8. An adenovirus according to Claim 7, wherein the viral promoter is selected from the group consisting of E1A, MLP, CMV and RSV LTR promoters.
9. A replication defective recombinant adenovirus according to Claim 1, comprising a cDNA sequence encoding
25 human pre-GDNF under the control of the RSV LTR promoter.
10. A replication defective recombinant adenovirus according to Claim 1, comprising a gDNA sequence encoding human pre-GDNF under the control of the RSV LTR promoter.
11. A replication defective recombinant adenovirus

according to Claim 1, comprising a DNA sequence encoding the whole, or an active part, of human glial cell-derived neurotrophic factor (hGDNF), or a derivative thereof, under the control of a tissue specific promoter enabling
5 expression in nerve cells.

12. A replication defective recombinant adenovirus according to Claim 11, wherein the promoter is the promoter of the neurone-specific enolase or the GFAP promoter.

10 13. An adenovirus according to Claim 1, lacking regions of its genome which are necessary for its replication in a target cell.

14. An adenovirus according to Claim 13, comprising the ITRs and a sequence enabling encapsidation, and in which
15 the E1 gene and at least one of the genes E2, E4 and L1-L5 is non-functional.

15. An adenovirus according to Claim 13, wherein said adenovirus is an Ad 2 or Ad 5 human adenovirus or a CAV-2 canine adenovirus.

20 16. A pharmaceutical composition comprising a replication defective recombinant adenoviruses according to Claim 1.

17. A pharmaceutical composition according to Claim 16, in an injectable form.

18. A pharmaceutical composition according to Claim 16,
25 comprising between 10^4 and 10^{14} pfu/ml of defective recombinant adenoviruses.

19. A pharmaceutical composition according to Claim 18, comprising between 10^6 to 10^{10} pfu/ml of defective recombinant adenoviruses.

20. A mammalian cell infected with one or more replication defective recombinant adenoviruses according to Claim 1.
21. A mammalian cell according to Claim 20, wherein said
5 cell is a human cell.
22. A mammalian cell according to Claim 20, wherein said cell is a human fibroblast, myoblast, hepatocyte, endothelial cell, glial cell or keratinocyte.
23. An implant comprising infected cells according to
10 Claim 20, and an extracellular matrix.
24. An implant according to Claim 23, wherein the extracellular matrix comprises a gel-forming compound.
25. An implant according to Claim 24, wherein the gel-forming compound is selected from the group consisting of
15 collagen, gelatin, glucoseaminoglycans, fibronectin and lectins.
26. An implant according to Claim 23, wherein the extracellular matrix further comprises a support for anchoring infected cells.
- 20 27. An implant according to Claim 26, wherein the support comprises polytetrafluoroethylene fibres.
28. A method of treating or preventing a neurodegenerative disease comprising administration to a patient suffering therefrom an effective amount of an
25 adenovirus according to Claim 1.
29. A method according to Claim 28, wherein said disease is selected from the group consisting of Parkinson's disease, Alzheimer's disease, Huntington's disease, and ALS.